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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/882,376	06/18/2001	John Peter Morseman	31676.0248	6731

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EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 02/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/882,376	MORSEMAN ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *November 13, 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *1 and 2* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 December 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12/03/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the claims

The amendment filed November 13, 2003 is acknowledged and has been entered.

Rejections Withdrawn

Claim Rejections – 35 U.S.C. 112 first paragraph

With respect to the claim rejections under 35 U.S.C. 112 first paragraph, Applicant argues that the definition of strongly chaotropic as supplied in the Applicants' specification (page 7, lines 4-13) provides sufficient guidance to one skilled in the art to select conditions in which the cross-linked allophycocyanin is not exposed to strongly chaotropic agent. Applicants arguments have been fully considered and found persuasive. The following rejections are withdrawn:

I. Claim 3 is rejected under 35 U.S.C. 112 first paragraph, as failing to comply with the written description requirement. With respect to the claim rejections under 35 U.S.C. 112 first paragraph, Applicant argues that the Examiner has misinterpreted 1 M sodium perchlorate as a strongly chaotropic agent. Applicant's arguments have been fully considered and found persuasive.

The following rejections are withdrawn:

II. Claims 3-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for sodium perchlorate, does not reasonably provide enablement for other strongly chaotropic agents

Claim Rejections 112 2nd paragraph

A. The deletion of the phrase "used according to this invention" from claim 3 has given greater clarity to the claim.

B. Applicants argument that strongly chaotropic agents is defined in the specification is found persuasive.

C. Applicants amendments and arguments directed to claims 4 and 9 are found persuasive.

Claim Rejections – 35 U.S.C. 103

With respect to the claim rejections under 35 U.S.C 103, Applicant argues that Ong teaches away from the Applicants invention. Since it is found persuasive that Applicants provide a definition for strong chaotropic agent. It is found persuasive that Ong teaches away from the Applicants invention because Ong uses 8 M Urea.

Rejections Maintained

Claim 3 the recitation "having the ability" is vague and indefinite.

Drawings

1. The drawings are objected to because there is no Figure 1 present in the application. The drawings begin with Figure 2 and end with Figure 7. It appears that Applicant has deleted Figure 1 or that Figure 1 is missing. The figures should be renumbered appropriately. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The

objection to the drawings will not be held in abeyance. Applicant is advised that no amendment in an application or the claims can introduce new matter.

Note: It is noted that Applicant corrected the numbering of Figures in the specification. However, Applicant failed to renumber the Figures in the corresponding drawings.

Specification

2. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Claims 11-14 recites distinct donor species. However, on page 9, line 25 – page 10, line 8 in the specification applicant discloses other donor/acceptor pairs. Applicant does not disclose distinct donor species.

3. Also, on page 19, line 4 of the specification. The disclosure "Figure 6" should be --Figure 5--.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 3-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 1M sodium perchlorate, does not reasonably provide enablement for any and all gentle chaotropic agents. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re W*ands USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to quantitating an analyte by measuring time resolved transfer of fluorescence energy to or from a label quantitatively associated with the analyte, the improvement comprising measuring the energy transferred from a donor compound having the ability to absorb light energy and then transfer this energy to cross-linked allophycocyanin in a time-resolved manner, where the cross-linked allophycocyanin has not been exposed to strongly chaotropic agents after cross-linking. The specification on page 7, lines 4-13 the applicant discloses that strongly denaturing chaotropic agents are defined herein as agents having more strongly denaturing effect than 1.5 sodium percholorate, and preferably as equivalent to 6M or greater urea or guanidine HCl. Instead of the strongly denaturing treatment used in preparation of XL-APC a more gently denaturant that does not affect the final 650/620 and 650/280 nm ratio is used to provide GL-APC, resulting in a fluorochrome more similar to the native

dye than the commercially available XL-APC. Typical denaturants which may be used in this format are sodium perchlorate, preferably at concentrations of about 1 M. However, it does not disclose the use of any and all gentle chaotropic agents. Furthermore, the use of gentle chaotropic agents on cross-linked allophycocyanin is not well known in the art and thus one of ordinary skill in the art would have a low level of predictability in the art.

The working examples in the specification are limited to the use of 1 M sodium perchlorate. At best, only 1M sodium perchlorate can be exposed to the cross-linked allophycocyanin not to affect the final 650/620 and 650/280 nm ratio as described in the specification. Such is not seen as sufficient to support the breath of the claims and one skilled in the art cannot practice the claimed invention without undue experimentation, because in order to not affect the final 650/620 and 650/280 nm ratio, one skilled in the art would have to have a high level of predictability, in order to successfully select a gentle chaotropic agent without undue experimentation.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 3-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 the recitation "having the ability" is vague and indefinite. The recitation is not a positive limitation. It does not constitute a limitation in any patentable sense.

Doe the donor compounds absorb light energy and then transfer this energy to cross-linked allophycocyanin in a time-resolved manner or not?

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 3-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al (homogenous Proximity Tyrosine Kinase Assays, Analytical biochemistry 269, 94-104 (1999)) in view of Applicant's statement regarding the sale of product (cross-linked allophycocyanin which had not been exposed to strongly chaotropic agents) (see IDS filed December 3, 2003).

Park et al disclose a method for quantitating an analyte by measuring time resolved transfer of fluorescence energy to or from a label quantitatively associated with analyte. Park et al disclose measuring the energy transferred from donor compounds to absorb light energy and then transfer this energy to cross-linked allophycocyanin. Park et al disclose the energy donor can be europium (abstract).

Park et al fail to specifically teach that the cross-linked allophycocyanin has not been exposed to strongly chaotropic agents after cross-linking, which is available for sale by Applicant more than one year prior to the filing date of this application.

Therefore, it would have been obvious to one of ordinary skill in the art to select the cross-linking agent as described in the statement provided by Applicant (see above) as an alternative for the cross-linking agent of Parks et al. And it appears both cross-linking agents would perform equally well in Time-Resolved Fluorescence Assays.

12. Claims 11-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al and Applicant's statement regarding the sale of product (cross-linked allophycocyanin which had not been exposed to strongly chaotropic agents) (see IDS filed December 3, 2003) in view of Applicant's admission of prior art.

Park et al and Applicant's statement differ from the instant invention in failing to specifically teach at least two distinct donor species present in different formats.

On page 9, lines 25 – page 10, line 8 in the specification Applicant discloses that the dye of this invention can be used with any known format for FRET. Applicant discloses the known formats. It would have been obvious to one of ordinary skill in the art to incorporate the cross-linked allophycocyanin of Applicant into different well known formats of FRET as disclosed by Applicant for quantitating an analyte by measuring time resolved fluorescence of a label quantitatively associated with the analyte.

Response to Arguments

112 2nd Rejections

13. Applicant's arguments filed November 13, 2003 concerning the recitation "having the ability to" have been fully considered but they are not persuasive.

Applicant argues that the phrase "having the ability" in claim 3 implies the positive property of the ability to absorb light energy. Further the claim specifically includes the limitations that the energy transfer be in a time resolved manner. This is not found persuasive because of reasons stated in the previous office action. It is recommended to delete the recitation "having the ability to" from the claim.

14. Applicant's arguments, see Amendment and remarks, filed November 13, 2003, with respect to the rejection(s)of claim(s) 3-6, 9 and 10 under U.S.C. 103 Park in view or Ong have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of IDS filed December 3, 2003 regarding applicants statement of the sale of

cross-linked allophycocyanin which had not been exposed to strongly chaotropic agents on or about December 22, 1998.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gary Counts
Examiner
Art Unit 1641
February 2, 2004

LONG V. LE
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02/05/04